

**Application No. 10/588,360
Amendment of August 10, 2011
Reply to Office Action of May 10, 2011**

REMARKS/ARGUMENT

This amendment responds under 37 C.F.R. § 1.116 to the Office Action of May 10, 2011.

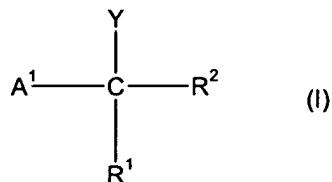
Claims 1 through 20 are pending in the application. Claims 1 through 8, 10, 15, and 20 are canceled. Claims 9, 11, 13, 14, 16, 18, and 19 are amended, and new claims 21 through 29 are added. No additional fee for claims is due.

Entry of these amendments is requested as it is believed they put the application in condition for allowance or in better condition for appeal.

1. Rejection under 35 U.S.C. § 103(a)

Claims 1 through 20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Cooke et al. (WO 01/11965) and Hubele (U.S. Patent No. 5,153,200) in view of HCAPLUS abstract 1995:694232 and Hopkinson et al. (U.S. Patent No. 6,746,988). The Applicants traverse this rejection and request reconsideration.

Cooke et al. claim a compound or a complex or salt thereof of the general formula I:



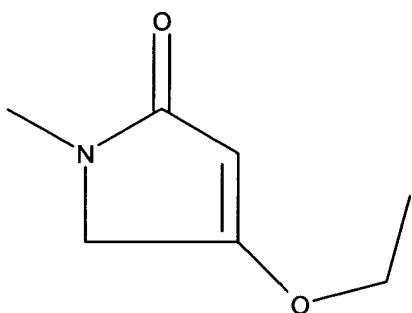
wherein:

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A^1 is 2-pyridyl substituted with from one to four moieties independently selected from the group consisting of halogen and trifluoromethyl, provided that at least one moiety is trifluoromethyl;

Y is a moiety selected from the group consisting of $-L-A^2$ and $-L^1-A^3$ wherein:

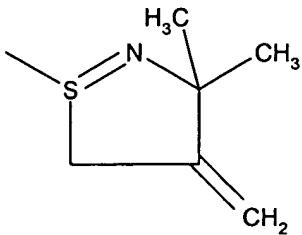
A^2 is selected from the group consisting of unsubstituted or substituted phenyl, cyclohexyl, cyclopropyl, thienyl, imidazolyl, tolyl, and



wherein any substituents on A^2 are independently selected from the group consisting of alkyl, halogen, and haloalkyl;

A^3 is selected from the group consisting of unsubstituted or substituted phenyl, pyridyl, thiodiazolyl, triazolyl, fluorenyl, tolyl, tetrazolyl, pyrimidinyl, imidazolyl, benzthiazolyl, quinolinyl, and

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wherein any substituents on A³ are selected from the group consisting of alkyl, halogen, haloalkyl, hydroxyl, and phenyl;

L is a 3-atom linker selected from the group consisting of -N(R⁵)C(=X)N(R⁶)-, -N(R⁵)C(=X)CH(R³)-, -CH(R³)N(R⁵)CH(R⁴)-, -CH(R³)N(R⁵)C(=X)-, -ON(R⁵)C(=X)-; wherein the left hand side of L is attached to the central carbon atom of formula I;

L¹ is a 4-atom linker selected from the group consisting of -N(R⁹)C(=X)X¹CH(R⁷)-, -N(R⁹)C(=X)CH(R⁷)CH(R⁸)-; -N(R⁹)C(R⁷)=C(R⁸)C(=X)-, -N(R⁹)C(=X)C(R⁷)(R⁸)SO₂-; and -N(R⁹)C(=X)C(R⁷)(R⁸)X¹; wherein the left hand side of L¹ is attached to the central carbon atom of formula I;

R¹, R², R³, and R⁴ are independently selected from the group consisting of hydrogen or alkyl;

R⁵, R⁶, R⁷, and R⁸ are independently selected from the group consisting of hydrogen, alkyl, and acyl;

X is selected from the group consisting of oxygen and sulfur;

X¹ is selected from the group consisting of oxygen and -N(R⁹)-; and

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R⁹ is selected from the group consisting of hydrogen and alkyl.

The Applicants acknowledge in the present specification that:

International patent application WO 01/11965 generically discloses numerous pyridylethylbenzamide derivatives. The possibility of combining one or more of these numerous pyridylethylbenzamide derivatives with known fungicidal products to develop a fungicidal activity is disclosed in general terms, without any specific example or biological data.

(U.S. Publication No. 2007/0137273, page 1, paragraph [0002].) It is true that the compounds of the present invention are structurally encompassed by the genus of Cooke et al., which is a very large genus, indeed.

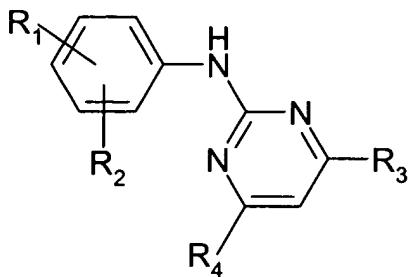
The Applicants also acknowledge that Cooke et al. disclose:

[0041] In addition, the composition can comprise one or more additional active ingredients, for example compounds known to possess plant-growth regulant, herbicidal, fungicidal, insecticidal, acaricidal, antimicrobial or antibacterial properties. Alternatively, the compound of the invention can be used in sequence with the other active ingredient.

However, there is no teaching or suggestion in Cooke et al. of any synergistic effect obtained when such pyridylethylbenzamide derivatives are combined with compounds capable of inhibiting methionine biosynthesis, nor is there any disclosure of what the ratios of the two fungicides should be, such as the currently claimed (A)/(B) weight ratio of from 0.01 to 20.

Hubele discloses compounds of the formula

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in which: R₁ and R₂ independently of one another are hydrogen, halogen, C₁-C₃ alkyl, C₁-C₂ haloalkyl, C₁-C₃ alkoxy or C₁-C₃ haloalkoxy; R₃ is hydrogen; C₁-C₄ alkyl; or C₁-C₄ alkyl substituted by halogen, hydroxy, or by cyano; cyclopropyl; or cyclopropyl mono- to tri-substituted by methyl and/or by halogen; and R₄ is C₃-C₆ cycloalkyl or C₃-C₆ cycloalkyl mono- to tri-substituted by methyl and/or by halogen. Cyprodinil is specifically disclosed. The compounds are said to have valuable microbical and insecticidal properties and to be useful in plant protection for preventing an attack on cultivated plants by phytopathogenic microorganisms. There is no disclosure or suggestion of using the combination of pyridylethylbenzamide derivatives with the compounds disclosed.

HCAPLUS abstract 1995:694232 discloses that cyprodinil is a fungicide and that its mode of action is inhibition of methionine biosynthesis. Again, there is no disclosure or suggestion of using the combination of pyridylethylbenzamide derivatives with cyprodinil.

Hopkinson et al. disclose surfactant systems comprising alkyl polyglycosides, anionic surfactants and basic compounds. Agricultural compositions comprising agriculturally active

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compounds, alkyl polyglycosides, anionic surfactants and basic compounds are disclosed. The surfactant systems and agricultural compositions may further comprise nonionic surfactants.

Hopkinson et al. fail to supplement the deficiencies of Cooke et al. and Hubele as references against the patentability of the subject invention, discussed above. At most, Hopkinson et al. teach that combinations of fungicides can be used in combination with surfactants. That this use is known in the art is also acknowledged. However, there is nothing in Hopkinson et al., alone or in combination with the other cited art, that would lead a person of ordinary skill in the art to prepare a composition comprising:

- (a) a pyridylethylbenzamide derivative of a specified formula and
- (b) a compound capable of inhibiting methionine biosynthesis;

in an (A)/(B) weight ratio of from 0.01 to 20.

It is understood to be the Examiner's position that the pyridylethylbenzamide derivatives are known fungicides and compounds that inhibit methionine biosynthesis are known fungicides and, thus, it would be obvious to use them in combination.

It is the Applicants' position, however, that they have discovered a combination in a particular ratio that clearly exhibits synergism and is neither disclosed nor suggested by the cited art. They have demonstrated this synergism for this combination in the examples of the present specification, using a means for determining synergism that is accepted in the art, i.e., the Colby formula, which was published in an article by S.R. Colby, "Calculation of the synergistic and

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antagonistic responses of herbicide combinations," 15 WEEDS 20-22 (1967). The Examiner's attention is directed to U.S. Patent No. 6,753,339 to Chazalet et al. in which the Colby method of determining synergism was also employed to the satisfaction of the Patent Office. In fact, the Applicants' representative searched the USPTO Patent Full-Text and Image Database using the keywords SPEC/Colby AND SPEC/synergism and obtained 214 hits. Clearly, the Colby method has been frequently used to the satisfaction of the USPTO to show synergism and, consequently, non-obviousness. Based on the teachings of the cited references, skilled artisans might have expected fungicidal activity for mixtures of the pyridylethylbenzamide derivatives and the compounds used with them in the practice of the present invention, but they would not have expected any synergy when associating these compounds, in particular, in the claimed weight ratio of from 0.01 to 20. Unexpected results are shown for the claimed combination, and it logically follows that the combination cannot be obvious.

More specifically, the term "synergistic effect" as used in this specification is understood to mean in particular that defined by Colby in the article cited above. This article uses the formula:

$$E = X + Y - (XY/100)$$

in which E represents the expected percentage of inhibition of a disease for a combination of the two fungicides at defined doses (for example, equal to x and y respectively), X is the percentage of inhibition observed for the disease by a first compound at a defined dose (equal to x), and Y is

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the percentage of inhibition observed for the disease by a second compound at a defined dose (equal to y). When the percentage of inhibition experimentally observed for the combination is greater than E, there is a synergistic effect.

In Example 1 of the present application:

X, the efficacy of N-{2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl}-2-trifluoromethylbenzamide (Compound 1) alone at a concentration of 500 g/ha is 25%; and

Y, the efficacy of cyprodinil alone at a concentration of 31.2 g/ha is 0%.

Thus, from the Colby formula, the expected efficacy of the combination of 500g/ha of N-{2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl}-2-trifluoromethylbenzamide and 31.2 g/ha of cyprodinil would be

$$E = 35 + 0 - [(35 \times 0) / 100], \text{ or}$$

$$E = 35 - 0, \text{ or}$$

$$E = 35\%$$

However, it has been shown experimentally that the actual efficacy of the combination is 55%.

Accordingly, by the Colby method, there is synergy in the unexpected increase in efficacy of 55% minus 35%, or 20%.

Similarly, in Example 2 of the present application:

X, the efficacy of N-{2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl}-2-trifluoromethylbenzamide (Compound 1) alone at a concentration of 37 ppm is 45%; and

Y, the efficacy of pyrimethanil alone at a concentration of 12.3 ppm is 90%.

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Thus, from the Colby formula, the expected efficacy of the combination of 37 ppm of N-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-trifluoromethylbenzamide and 12.3 ppm of pyrimethanil would be

$$E = 45 + 90 - [(45 \times 90) / 100], \text{ or}$$
$$E = 135 - 40.5, \text{ or}$$
$$E = 94.5\%.$$

However, it has been shown experimentally that the actual efficacy of the combination is 100%. Accordingly, by the Colby method, there is synergy in the unexpected increase in efficacy of 100% minus 94.5%, or 5.5%.

Further, in Example 3 of the present application:

X, the efficacy of N-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-trifluoromethylbenzamide (Compound 1) alone at a concentration of 500 g/ha is 40%; and
Y, the efficacy of mepanipyrim alone at a concentration of 500 g/ha is 0%.

Thus, from the Colby formula, the expected efficacy of the combination of 500 g/ha of N-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-trifluoromethylbenzamide and 500 g/ha of mepanipyrim would be

$$E = 40 + 0 - [(40 \times 0) / 100], \text{ or}$$
$$E = 40 - 0, \text{ or}$$
$$E = 40\%.$$

However, it has been shown experimentally that the actual efficacy of the combination is 70%. Accordingly, by the Colby method, there is synergy in the unexpected increase in efficacy of 70% minus 40%, or 30%.

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In the current Office Action, the Examiner calls the Applicants' attention to a decision of the Board of Patent Appeals and Interferences, *Ex parte Quadranti*, 25 U.S.P.Q.2d 1071, 1072-73 (Bd. Pat. App. & Int. 1992). The BPAI in that case said, "On the issue of whether or not synergism has been demonstrated, generalizations such as the Colby formula are not particularly useful," and "[T]he Colby formula test . . . is at best controversial and in our view *probably* invalid . . ." (emphasis added). This language falls short, it is submitted, of rejecting the argument that the Colby method is a valid method for calculating patentable synergism.

Furthermore, the *Quadranti* case was decided on May 22, 1992. Recently, the Applicants' representative searched the USPTO Patent Full-Text and Image Database using the keywords SPEC/Colby AND SPEC/synergism and obtained 225 hits. That is, 225 patents referring to synergism and the Colby method have issued since 1976, the beginning of the database. Of these 225 issued patents, 186 have issued *since* May 22, 1992, the date of the *Quadranti* decision. On this basis alone, the USPTO is abundantly familiar with the Colby method and the holding in *Quadranti*, and, notwithstanding, has frequently issued patents employing such data.

It is therefore requested that rejection of claims 1 through 19 under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Cooke et al. and Hubele in view of HCAPLUS abstract 1995:694232 and Hopkinson et al. be withdrawn.

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2. Rejection on the Ground of Non-statutory Obviousness-type Double Patenting

Claims 1 through 20 are rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1 through 12 of U.S. Patent No. 7,776,892 to Grosjean-Cournoyer et al. As pointed out in the Office Action, a timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application.

The present application and U.S. Patent No. 7,776,892 are commonly owned by BAYER CROPSCIENCE A.G.

A Terminal Disclaimer Under 37 C.F.R. § 1.321 (c) disclaiming, with the customary exceptions, the terminal part of the statutory term of any patent granted on the instant application that would extend beyond the expiration date of the full statutory term of U.S. Patent No. 7,776,892 will be filed upon an indication of allowability.

Accordingly, the Applicants will request that rejection of claims 1 through 20 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1 through 12 of U.S. Patent No. 7,776,892 be withdrawn.

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In view of the foregoing, it is submitted that this application is in condition for allowance.

Favorable consideration is requested.

Respectfully submitted,



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